INTRODUCTION

Concern about decreased fetal movements (DFM) leads to presentation at maternity services in up to 15% of pregnancies and DFM presentation is associated with subsequent adverse pregnancy outcomes including stillbirth and fetal growth restriction. Case control studies have demonstrated an association between DFM and stillbirth after 28 weeks' gestation and several studies have demonstrated links between DFM and placental pathology. Observational studies have also reported associations between DFM and other adverse neonatal outcomes including fetomaternal hemorrhage, neurodevelopmental disability (including a lack of response to therapeutic hypothermia), and structural abnormalities such as neuromuscular congenital abnormalities. These associations support a causal relationship between DFM and adverse outcome. Plausible mechanisms have been suggested: a reduction in fetal activity represents a compensatory measure to save energy at a time of oxygen or nutrient stress for the fetus, which may then...
resolve (or not), and a persistent shortage of oxygen or nutrients will lead to absent fetal movements.\textsuperscript{11}

However, DFM presentations are common and in most instances the pregnancy outcome is normal.\textsuperscript{12,13} Systematic reviews of intervention studies aiming to improve pregnancy outcomes by evaluating interventions that raise DFM awareness\textsuperscript{14–16} and/or interventions for the clinical management of DFM\textsuperscript{17} show that the evidence is uncertain about their effects on stillbirth.\textsuperscript{18–20} The effect size of the association between DFM and stillbirth is moderate; a recent individual patient data meta-analysis of five studies gave an adjusted odds ratio (aOR) of 2.33 (95% CI: 1.73–3.14).\textsuperscript{21} There is an apparent gradient in this effect, with women presenting with recurrent DFM at greater risk of stillbirth than those who have a single episode of DFM (aOR for women with recurrent DFM 5.11 [95% CI: 3.22–8.10]).\textsuperscript{22} Therefore, further studies are needed to determine whether reductions in stillbirth can be achieved by fetal movement awareness and management of DFM presentations.

Several issues pertaining to DFM need to be addressed and have been discussed during the workshop:

1. Evidence for fetal movement education to reduce stillbirths
2. Development of a core outcome set (COS) for studies of interventions for DFM
3. Risk of adverse outcomes related to placental dysfunction in women with DFM
4. Monitoring management strategy using Doppler abnormalities (the CEPRA study)\textsuperscript{23}
5. The role of a Kleihauer Betke test in case of DFM
6. What information should be given to pregnant women regarding fetal movement?

\section{The Evidence for Fetal Movement Education Interventions to Reduce Stillbirths}

Promoting awareness of fetal movements via kick counting was commonly practiced in the 1970s and 1980s. Publication of the landmark Grant et al. cluster randomized controlled trial involving 68,000 women in 1989 which showed that routine kick counting when compared to standard care did not reduce stillbirths, effectively cooled efforts to promote fetal movement awareness in both research and clinical practice.\textsuperscript{15} However, the Grant et al. trial was noted to have some limitations, including contamination, low fidelity of the intervention and lack of a management protocol for women who presented with DFM.\textsuperscript{1} For example, a high proportion of women in the control group were also asked to count kicks and amongst women in the intervention group compliance with the counting protocol was low with just 60% completing daily counting. Furthermore, more women with stillbirth in the intervention group presented at hospital with a fetal movement concern and a live fetus, but due to lack of effective management subsequent fetal deaths were not averted. However, the trial did show a 30% reduction in the stillbirth rate over the duration of the study (relative to the background population rate) and increased awareness of DFM across the study population was postulated as the possible reason.\textsuperscript{15}

A Norwegian team published a before-and-after analysis of implementation of a fetal movement quality improvement initiative in more than 65,000 women.\textsuperscript{24} This initiative included an information brochure for women, with optional kick counting, combined with a clinical assessment protocol for healthcare providers recommending universal ultrasound for assessment of DFM. A significant reduction in stillbirths from 4.2% to 2.4% was seen in women with DFM. However, transferability to other settings needed to be assessed by further trials.

Recently, two large cluster randomized trials have attempted to definitively answer the question of the role of education for women and their health care providers about DFM. In the UK, the “awareness of fetal movement and care package to reduce fetal mortality (AFFIRM) trial” was implemented across 33 hospitals with over 400,000 women.\textsuperscript{25} While in Australia and New Zealand, My Baby’s Movements (MBM) was implemented across 26 sites including almost 300,000 women.\textsuperscript{16} AFFIRM provided a new brochure for women and a new clinical protocol that involved a low threshold for induction of labor for DFM. MBM promoted an existing fetal movement brochure for women and a mobile phone app with optional kick counter and daily alerts. Both studies included clinician education and were powered to detect a 30% reduction on stillbirths.

AFFIRM reported a small reduction in stillbirths (point estimate = 12%) that did not reach statistical significance, and an increase in cesarean sections, inductions of labor and neonatal unit stays of >48h.\textsuperscript{17} Similarly, the MBM trial showed a small nonsignificant reduction in stillbirth, albeit with no increase in obstetric intervention or adverse neonatal outcome. Both trials had limitations. However, observational data from MBM did show a 27% reduction in stillbirths across the participating hospitals, over the 3-year period of the trial. The MBM trial was undertaken at a time of increasing attention to stillbirth across Australia so this reduction may be due to general increasing awareness and attention to fetal movements although this may be due other single or combined practice improvement efforts.

In another cluster-randomized controlled trial (n = 39,865) of raising awareness of fetal movements in Sweden, maternity clinics were randomized to the Mindfetalness method or to routine care.\textsuperscript{14} When practicing Mindfetalness, the pregnant woman focuses on the strength, character, and frequency of the movements (without counting) daily, from 28 weeks’ gestation, whilst lying on her side at a time when the baby is awake. Compared to routine care group, fewer women in the Mindfetalness group had a cesarean section, induction of labor, babies transferred to neonatal care or born small for gestational age. However, no differences were seen regarding Apgar score of less than seven at 5 min (including Apgar of 0, i.e., stillbirths). More women sought care due to DFM in the Mindfetalness group, 6.6%, compared to 3.8%, in the routine care group. During the trial, the stillbirth rate decreased from 3.5–4.0/1000 births to 2.9/1000 births. Pregnant women had a positive attitude to Mindfetalness.
and the majority practiced the method daily. Midwives also found distributing Mindfetalness leaflets was supportive of their work.25 In summary, trials of fetal movement awareness interventions have yet to demonstrate a significant impact on stillbirth rates. However, large scale trials of complex educational interventions are problematic, and it should be noted that existing trials have all compared fetal movement awareness interventions with routine care that invariably also involves fetal movement awareness, making it difficult to measure effects. Promoting fetal movement awareness may yet prove beneficial, although caution is required to avoid harm associated with (unnecessary) intervention. Determining optimal approaches to education around fetal movements and assessment of such cases remains a research priority.

3 | DEVELOPMENT OF A CORE OUTCOME SET FOR STUDIES OF DFM

Core outcome sets (COS) describe standardized sets of outcomes that should be measured and reported in all studies in a specific area as a minimum.26 There is not currently a COS for studies of DFM and published studies of interventions for DFM do not all measure the same outcomes, which makes evidence synthesis difficult and means that guidelines are not informed by all the evidence. This study aims to identify the most important outcomes in studies of DFM to improve future reporting and data synthesis of studies in this area; this will be relevant to studies that aim to encourage awareness of fetal movements and/or those that aim to evaluate interventions for the subsequent clinical management of DFM.27 A systematic review of the literature was conducted to identify outcomes measured by in randomized and non-randomized studies that aimed to raise awareness of DFM (for example by using mindfulness techniques, fetal movement counting, or other tools such as leaflets or mobile phone applications) and/or that evaluated the clinical management of DFM.18 Full inclusion criteria are described in Table 1.

<table>
<thead>
<tr>
<th>Population</th>
<th>Singleton pregnancies presenting at least once in a maternity care setting after 28 weeks’ gestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Any intervention aimed at raising awareness of DFM and/or evaluating the clinical management of DFM</td>
</tr>
<tr>
<td>Comparator</td>
<td>Any other intervention described above or no intervention</td>
</tr>
<tr>
<td>Outcome</td>
<td>Any maternal or fetal outcomes</td>
</tr>
<tr>
<td>Study design</td>
<td>Controlled randomized and non-randomized studies with clearly reported mechanism of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment</td>
</tr>
</tbody>
</table>

Table 1 | Inclusion criteria for systematic review.

Eligible participants were: (1) Lay experts - anyone who is or has been pregnant, and their partners if applicable. (2) Researchers involved in work related to DFM. (3) Clinicians with experience of DFM. Participants were recruited by emailing study authors, advertising on social media, and snowball sampling. Methods are described in full in the study protocol.24 The final COS aims to ensure that the most relevant outcomes are measured by future studies as well as improving the reporting and synthesis of these studies.

4 | RISK OF ADVERSE OUTCOMES AND PLACENTAL DYSFUNCTION IN WOMEN WITH REDUCED FETAL MOVEMENTS

Exploration of physiological mechanisms behind DFM and developing fetal compromise is critical for advancing knowledge in this area. Applying the model where DFM is a fetal response to oxygen and/or nutrient deprivation it can be hypothesized that evidence of placental dysfunction should be more prevalent in such cases. Warrander et al. conducted a case control study of 36 placentas from women who gave birth within 7 days of presentation with DFM and 36 women with no history of DFM.28 Placentas from women with DFM were smaller and more likely to have an off-center cord insertion. Microscopically, placentas from women with DFM more often had signs of maternal vascular malperfusion (MVM): more syncytial knots, fewer fetal blood vessels and a smaller trophoblast area. Further analysis of these samples showed increased inflammatory cells consistent with sterile inflammation. These structural changes were associated with a reduction in System A amino acid transport in women with DFM. These changes are similar to those observed in pregnancies with overt fetal growth restriction.

Two studies have examined histopathological features of placentas in women with DFM. Winje et al. studied 129 women with DFM and 191 controls; while DFM was not linked to the presence...
of any placental pathology (OR 1.3, 95% CI: 0.8–2.2) it was associated with MVM (OR 3.5, 95% CI: 1.1–11.3). Levy et al. examined placentas from 203 women with DFM (with an interval 2 weeks or less before birth) and 203 controls. Finding a greater proportion of women with DFM had a small placenta (10th percentile (22.6% vs. 3.9%, P < 0.001), MVM (30.5% vs. 18.7%, P = 0.007), and maternal inflammatory response (43.3% vs. 29.5%, P = 0.005). This association was confirmed when examining cases of stillbirth in a retrospective cohort study of cases of stillbirth found that pregnancies with RFM prior to diagnosis of stillbirth were independently associated with placental insufficiency (aOR 2.79, 95% CI: 1.0.16–5.04) and were less frequently associated with maternal proteinuria (OR 0.16, 95% CI: 0.07–0.62) and previous pregnancy loss <24 weeks (OR 0.20, 95% CI: 0.07–0.70).28

Taken together these placental studies provide a biological basis to understand the association between DFM and adverse perinatal outcomes relating to perinatal asphyxia attributable to placental insufficiency.

5 | MONITORING MANAGEMENT STRATEGY BASED ON DOPPLER ABNORMALITIES: CEPRA STUDY

Assessment of fetal wellbeing in late pregnancy often does not accurately identify a fetus at risk for adverse outcomes, which results in considerable “over treatment” of women with healthy fetuses whilst the truly compromised fetuses often remain undetected. The cerebroplacental ratio (CPR – the ratio of the umbilical artery pulsatility index over the middle cerebral artery pulsatility index) is indicative of suboptimal fetal growth and placental insufficiency and a marker of adverse outcomes.29 Abnormal Doppler indices in DFM are associated with adverse perinatal outcomes.

It is unknown whether expedited birth, indicated by an abnormal Doppler, can improve adverse outcomes in women with DFM. This question is currently being investigated in the CEPRA trial.23 The CEPRA is a multicenter international cluster randomized clinical trial of women with singleton pregnancies with reduced fetal movements at term randomized to Doppler measurements that are either an unblinded or blinded arm for the healthcare professional. Only women with an estimated fetal weight >10th centile and normal cardiotocograph (CTG) are eligible. Expedited birth is pursued in women with a low CPR in the unblinded arm. Women in the blinded arm will not have their CPR results revealed for clinical decision making and will receive routine clinical care. The findings of this trial will help to inform clinical management of women presenting with DFM. The primary aim of this study is to assess whether expedited birth of women with DFM identified as high risk based on a low CPR improves neonatal outcomes.

The role of interventions related to an abnormal CPR in small for gestational age fetuses at (near) term has been or is currently being assessed in three trials: the DRIGITAT study,30 TRUFFLE 2,31 and RATIO 37.32 The CEPRA study is recruiting women in pregnancies with appropriate for gestational age (AGA) fetuses with reduced fetal movements as an early sign of placental insufficiency. The primary outcome is a composite of severe neonatal outcomes including perinatal death. Secondary aims include measurement of childhood outcomes, development of maternal hypertensive disorders, and the predictive value of serum biomarkers for adverse outcomes when stratified by CPR. Trials of promoting fetal movement awareness have yet to demonstrate effective reduction in stillbirths. The ongoing CEPRA trial will help to elucidate approaches to fetal assessment of DFM presentations.

6 | THE ROLE OF A KLEIHAUER BETKE TEST IN CASES OF DFM

Investigations for fetomaternal hemorrhage (FMH) are recommended in some clinical practice guidelines as part of the clinical evaluation of DFM.33 Maternal reports of decreased or absent fetal movements are the most common presenting symptom of FMH.34 In a case series of 24 neonates with severe anemia and a history of FMH, 54% had decreased or absent fetal movements.34 However, FMH occurs in an estimated 0.3% of live births, and massive FMH accounts for only about 4% of stillbirths and 0.4% of neonatal deaths.35,36 In principle, early detection of FMH may allow for stillbirths and adverse neonatal outcomes due to fetal anemia to be reduced. In practice, detection of FMH before it leads to adverse consequences for the fetus or neonate is complex.

When FMH is suspected, testing can be conducted for fetal cells in maternal blood, or for fetal anemia. Small volumes of blood loss are unlikely to cause important fetal anemia or stillbirth. The amount that has been considered significant for causing fetal death has been described as somewhere between 80 and 150 mL at term or >20 mL/kg.38 In 99% of FMH cases volume of blood loss is less than 15 mL.38 The degree of fetal compromise in FMH is dependent on the volume of blood lost in relation to fetal size and whether the bleeding is chronic or from a single event. Fetal cells last around 100 days in the maternal circulation, and so there is no way to know if a positive result is a new event or a past event that has resolved.

Testing for fetal cells in maternal blood can occur using the Kleihauer Betke test (KBT) or flow cytometry. The KBT is the most commonly used test worldwide and is based on fetal hemoglobin resistance to acid elution.35 After staining, adult cells are seen as "ghosts" on the blood film, while fetal red blood cells remain intact, appearing bright pink. The KBT is a labor-intensive test requiring a skilled laboratory technician to stain and count fetal cells under the microscope – results may not be available “after-hours” or may require a technician to be called in. Unfortunately, there is also significant variability between laboratories, and false positive results due to maternal hemoglobinopathy.38,39 Overall, the KBT tends to overestimate the volume of FMH and may not be informative of fetal anemia. A retrospective cohort study reported that fetal outcomes associated with FMH were not significantly different between those with negative and those positive KBT results.40
Fetal anemia may be revealed by an abnormal CTG, particularly a sinusoidal fetal heart rate pattern, or by Doppler assessment of the peak systolic velocity of blood flow in the middle cerebral artery (MCA PSV). To perform the MCA PSV the sonographer requires experience at obstetric ultrasound, and even in the best hands there is a high false positive rate in a low prevalence setting. Published reports on screening of women with risk factors for FMH have found that in the majority of cases of FMH and fetal compromise the CTG was also abnormal.40,41

In conclusion, although maternal report of DFM can be a sign of FMH, presentations for DFM are common in maternity care and most do not involve FMH. KBT is costly, not a reliable indicator of fetal anemia and may drive unnecessary intervention when tests are positive for small hemorrhages. Fetuses with significant anemia will have an abnormal CTG in most cases, thus this should be used as the primary screening test.

7 | FETAL MOVEMENT CONVERSATIONS: INFORMATION-SHARING DURING PREGNANCY

This part of the symposium addressed sharing of information about fetal movement as part of pregnancy care. As mentioned previously, it has been established that DFM is associated with stillbirth and with fetal growth restriction;1 however, there is a lack of high-quality evidence to guide best practice in this area.19 Maternity care providers are encouraged to inform pregnant women about the importance of being aware of fetal movements. Yet, studies suggest the information shared is often not evidence-based and women would like more information about normal fetal movements and what to expect.52

In this session an educative approach based on sharing gestation-appropriate information about what fetal movements to expect was promoted, beginning at 20 weeks’ gestation. This approach is informed by studies of maternally perceived fetal movements in pregnancies with normal outcome and pregnancies with stillbirth.21,43,44

Fetal movement features associated with ongoing pregnancy include increasing strength of movements, the presence of occasional or daily fetal hiccups, and a pattern of moderate or strong movements in the evening.3,21 A healthy fetus near term will have longer periods of time when they are quiet due to reduced intrauterine space and neurological development, but will still have a pattern of strong or moderate movement in the evening and will move every day.43,45

Fetal movement features associated with stillbirth include decreased frequency, decreased strength, and a fetus that is quiet in the evening.4 Decreased frequency is more strongly associated with stillbirth preterm, particularly 28–32 weeks’, while a single episode of unusually vigorous movement is modestly associated with stillbirth near term.21

Informing women about normal fetal movement features and asking about their own baby’s usual movement strength, frequency and pattern empowers women to reassure themselves when their baby is well and to seek help when movements are altered. Healthcare providers can help to achieve this by asking simple questions such as: “Tell me about your baby’s movements?”, “Are baby’s movements as strong as usual?”, “Is your baby as active as usual?”, “When is your baby most active?”. Women should be informed that a healthy fetus can be felt moving every day. Absence of movements for a day, or a significant reduction in strength or frequency of movements for a day or more warrants a check-up.24 If it is evening and fetal movements have not been perceived, the woman should not put off attending until the following day. An important caveat to this approach is for health care providers to appreciate that pregnant women with a stillbirth may express their concern in a variety of ways and sometimes only as a sense that something is wrong. All women with a subjective concern about fetal movements should be assessed promptly.

8 | CONCLUSION

Trials of fetal movement awareness interventions have yet to demonstrate a significant impact on stillbirth rates. However, demonstrating benefits for fetal movement awareness in clinical trials is difficult due to risk of contamination such as fetal movement awareness amongst control groups, and variation in guidelines for management of DFM. Policy makers should be aware that DFM remains an indicator of possible fetal compromise and clinical evaluation is warranted. Mounting evidence from placental studies supports a physiological basis for the association of DFM and placental insufficiency as a causative mechanism for stillbirth and clinical assessment protocols should account for this. Further studies are needed to inform management of higher risk DFM subgroups including those with DFM in early third trimester and those with recurrent presentation. Assessment of fetal wellbeing near term is difficult and the findings of future trials to determine the role of Doppler studies to guide timing of birth are keenly awaited. A core outcome set for fetal movement research has recently been developed which will improve future reporting of clinical trials and synthesis of findings.

Promoting fetal movement awareness may yet prove beneficial, although caution is required to avoid harm associated with unnecessary intervention. Regardless of efforts to promote fetal movement awareness women will present with DFM. We advise sharing information with pregnant women about the importance of perception of regular, daily fetal movements in the third trimester as a sign of fetal wellbeing. The clinical practice guideline developed by the Stillbirth Center of Research Excellence in Australia provides the most current and comprehensive evidence-based guidance on clinical management of DFM.46 Proactively asking about fetal movement strength, frequency, and pattern as part of antenatal care is likely to be more satisfying for pregnant women and allows for a more nuanced assessment of fetal behavior. Adapting our understanding of optimal testing approaches to identify fetuses at risk amongst those presenting with DFM remains a research priority.
AUTHOR CONTRIBUTIONS
Vicki Flenady conceived of the workshop contributions and Sanne J. Gordijn conceived the report. The first draft was prepared by Billie F. Bradford and Dexter J. L. Hayes. All authors contributed to the manuscript, revised the manuscript, and have approved its submission.

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